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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,931	10/11/2005	Myra Gilligan	T1629YP	6852

210 7590 10/11/2007

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P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
O DELL, DAVID K	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
10/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,931	GILLIGAN ET AL.	
	Examiner	Art Unit	
	David K. O'Dell	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-19* is/are pending in the application.

4a) Of the above claim(s) *17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *10 and 12-16* is/are rejected.

7)☒ Claim(s) *11 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 11 October 2005
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 10-19 are pending in the current application. Claims 17-19 are withdrawn from consideration as being drawn to a non-elected invention. Claims 10-16 are under examination.

2. This application is a 371 of PCT/GB04/01998 filed 05/07/2004, which claims priority to Great Britain application 0311349.5 filed 05/16/2003.

Response to Restriction/Election

3. A telephone call was placed to applicant's representative Mr. Eric Thies on September 27, 2007 regarding a two-way restriction requirement between the compounds and compositions (claims 10-16) and the methods of treatment (claims 17-19). The compound Group I was elected without traverse. The applicant was advised as to the right of rejoinder of withdrawn process claims.

Group I, Claims 10-16 drawn to compounds and compositions having a piperdinyl-sulfone core.

Group II, Claims 17-19 drawn to methods of treatment with the compounds of Group I.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is *presented prior to* final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be **allowable**, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai; In re Brouwer and 35 U.S.C.§ 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to

maintain dependency on the product claims or to otherwise include all the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01. Filing of appropriate terminal disclaimer in anticipation of a rejoinder may speed prosecution and the process of rejoinder.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 10, 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fletcher, S. R. et. al. "4-(Phenylsulfonyl)piperidines: Novel, Selective, and Bioavailable 5-HT2A Receptor Antagonists." *Journal of Medicinal Chemistry*, **2002**, *45*, 492-503 (cited on IDS) AND Ackermann et. al. WO 2001/51469 (cited on IDS) AND Blurton, et. al. WO 2000/043362 (cited on IDS) AND Wang, H. et. al. "Synthesis and biological activities of new 5-HT2A selective ligands N-substituted-piperidinyl-4-phenylthioether and sulfone derivatives." *Yaoxue Xuebao*, **2001**, *36*, 274-277, (abstract only), in view of Patani et. al. "Bioisosterism: A Rational Approach in Drug Design" *Chemical Reviews* **1996**, *96*, 3147-3176. The claims are drawn to compounds where Ar is phenyl, n is 1 or 0, m is 0 or 1 and W is (C=O) or CH2, with the various Q and R1-R4 definitions as below in the fifty or so compounds of Ackermann, Blurton, Fletcher, and Wang. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459

(1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

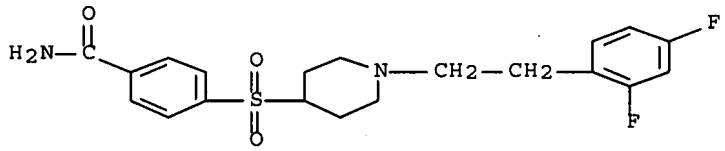
Determination of the scope and content of the prior art

(MPEP 2141.01)

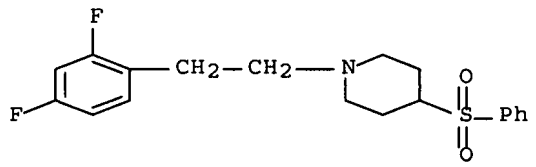
Fletcher, Ackerman, Blurton, and Wang et. al. teach compounds that are position isomers of the compounds of the instant case, alternatively these compounds can be seen as bioisosteric replacements of hydrogen atom with fluorine atom. These compounds have the same activity namely at the 5HT2a receptor.

In particular Fletcher teaches the following compounds:

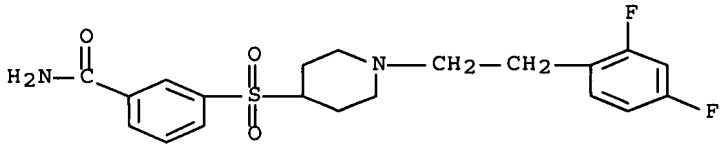
RN 285994-74-3 CAPLUS
CN Benzamide, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



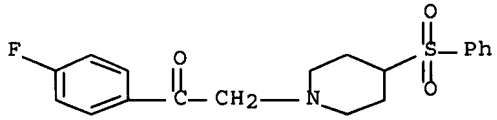
RN 285994-92-5 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-(phenylsulfonyl)- (9CI) (CA
INDEX NAME)



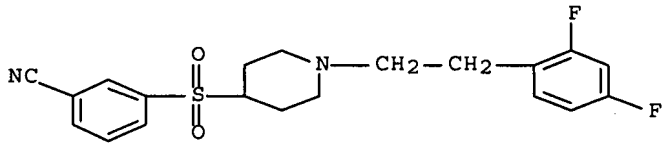
RN 285994-94-7 CAPLUS
CN Benzamide, 3-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-
(9CI) (CA INDEX NAME)



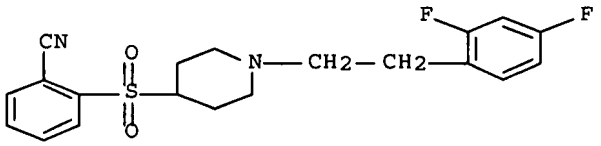
RN 285994-99-2 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-[4-(phenylsulfonyl)-1-piperidinyl]- (9CI)
(CA INDEX NAME)



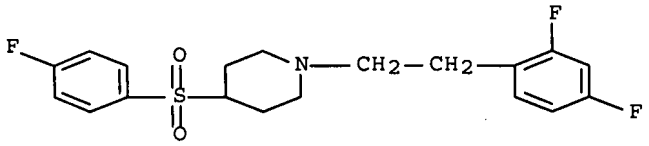
RN 400729-07-9 CAPLUS
CN Benzonitrile, 3-[[1-[2-(2,4-difluorophenyl)ethyl]-4-
piperidinyl]sulfonyl]-
(9CI) (CA INDEX NAME)



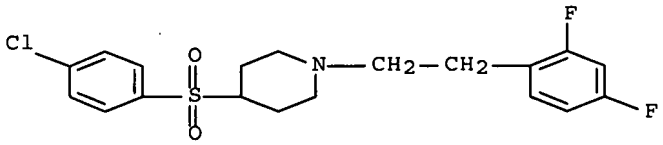
RN 400729-08-0 CAPLUS
CN Benzonitrile, 2-[[1-[2-(2,4-difluorophenyl)ethyl]-4-
piperidinyl]sulfonyl]-
(9CI) (CA INDEX NAME)



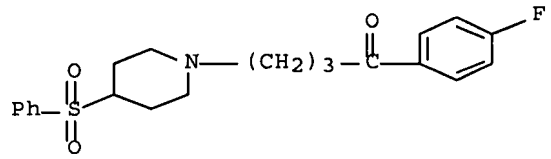
RN 400729-09-1 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[(4-fluorophenyl)sulfonyl]-
(9CI) (CA INDEX NAME)



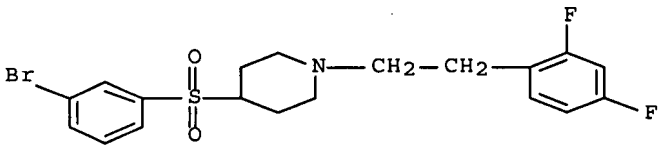
RN 400729-10-4 CAPLUS
CN Piperidine, 4-[(4-chlorophenyl)sulfonyl]-1-[2-(2,4-difluorophenyl)ethyl]-
(9CI) (CA INDEX NAME)



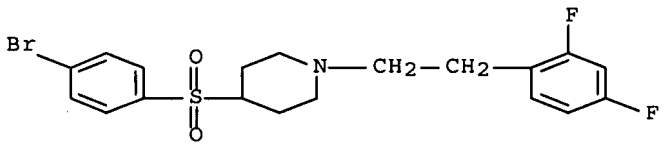
RN 400729-13-7 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-[4-(phenylsulfonyl)-1-piperidinyl]-
(9CI)
(CA INDEX NAME)



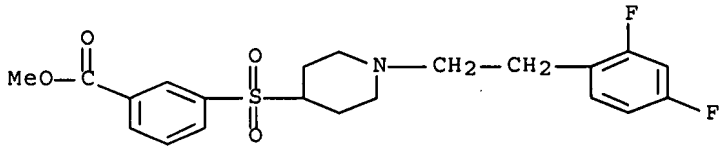
IT 285995-09-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure activity of 4-(phenylsulfonyl)piperidines as
novel, selective, and bioavailable 5-HT2A receptor antagonists)
RN 285995-09-7 CAPLUS
CN Piperidine, 4-[(3-bromophenyl)sulfonyl]-1-[2-(2,4-difluorophenyl)ethyl]-
(9CI) (CA INDEX NAME)



IT 285995-02-0P 285995-10-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and structure activity of 4-(phenylsulfonyl)piperidines as
novel, selective, and bioavailable 5-HT2A receptor antagonists)
RN 285995-02-0 CAPLUS
CN Piperidine, 4-[(4-bromophenyl)sulfonyl]-1-[2-(2,4-difluorophenyl)ethyl]-
(9CI) (CA INDEX NAME)

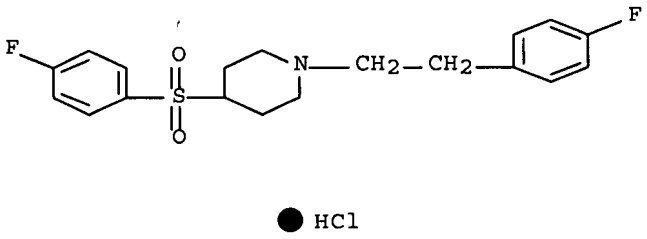


RN 285995-10-0 CAPLUS
CN Benzoic acid, 3-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-
, methyl ester (9CI) (CA INDEX NAME)

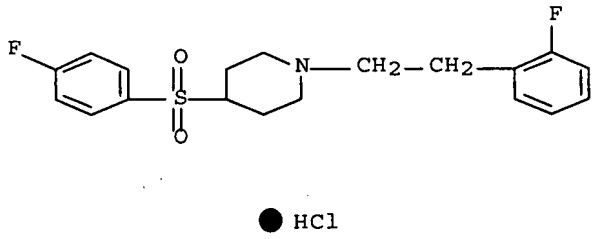


Ackermann et. al. teaches more of the same compounds:

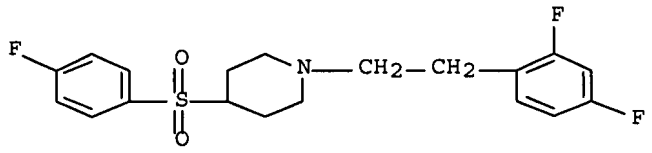
RN 349664-80-8 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(4-fluorophenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



RN 349664-81-9 CAPLUS
CN Piperidine, 1-[2-(2-fluorophenyl)ethyl]-4-[(4-fluorophenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)

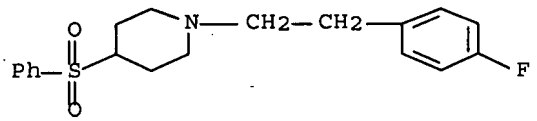


RN 349664-82-0 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[(4-fluorophenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



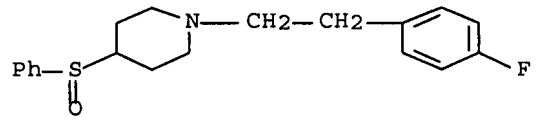
● HCl

RN 349664-83-1 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-(phenylsulfonyl)-, hydrochloride
(9CI) (CA INDEX NAME)



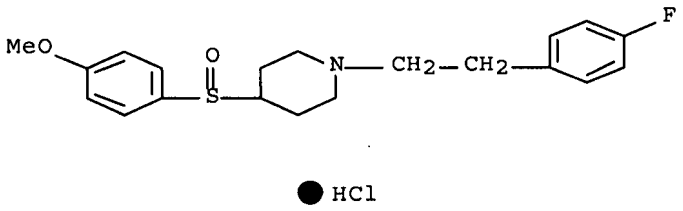
● HCl

RN 349664-84-2 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-(phenylsulfinyl)-, hydrochloride
(9CI) (CA INDEX NAME)

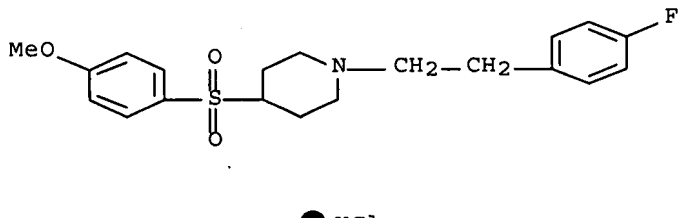


● HCl

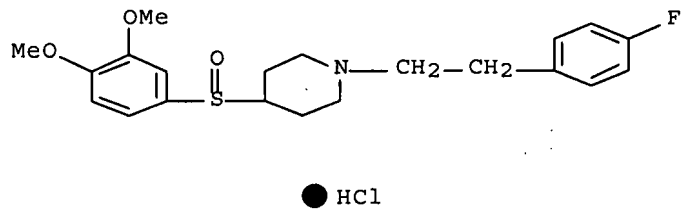
RN 349664-87-5 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(4-methoxyphenyl)sulfinyl]-, hydrochloride (9CI) (CA INDEX NAME)



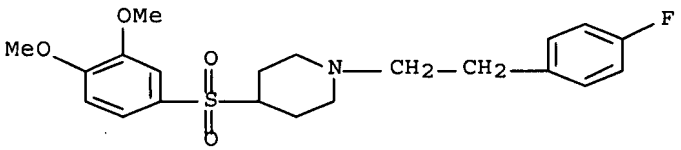
RN 349664-88-6 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(4-methoxyphenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



RN 349664-89-7 CAPLUS
CN Piperidine, 4-[(3,4-dimethoxyphenyl)sulfinyl]-1-[2-(4-fluorophenyl)ethyl]-
, hydrochloride (9CI) (CA INDEX NAME)

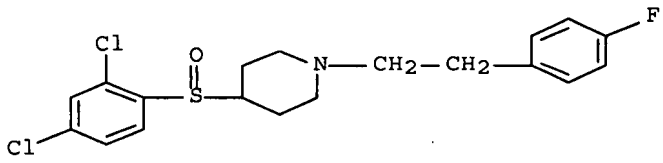


RN 349664-90-0 CAPLUS
CN Piperidine, 4-[(3,4-dimethoxyphenyl)sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-
, hydrochloride (9CI) (CA INDEX NAME)



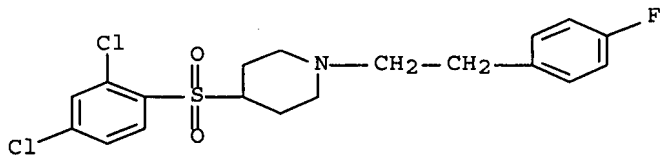
● HCl

RN 349664-91-1 CAPLUS
CN Piperidine, 4-[(2,4-dichlorophenyl)sulfinyl]-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

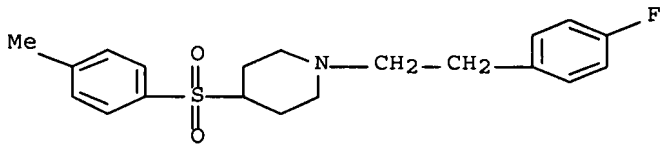
RN 349664-92-2 CAPLUS
CN Piperidine, 4-[(2,4-dichlorophenyl)sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

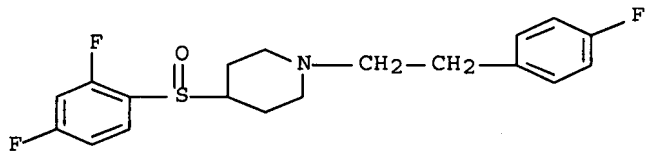
RN 349664-94-4 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(4-methylphenyl)sulfonyl]-,

hydrochloride (9CI) (CA INDEX NAME)



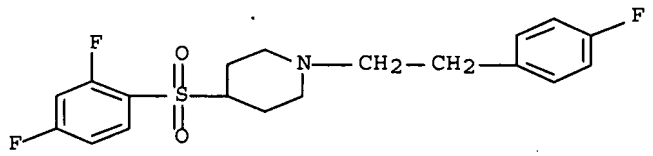
● HCl

RN 349664-95-5 CAPLUS
CN Piperidine, 4-[(2,4-difluorophenyl)sulfinyl]-1-[2-(4-fluorophenyl)ethyl]-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

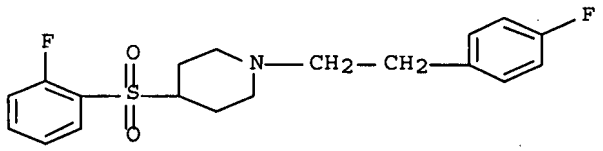
RN 349664-96-6 CAPLUS
CN Piperidine, 4-[(2,4-difluorophenyl)sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

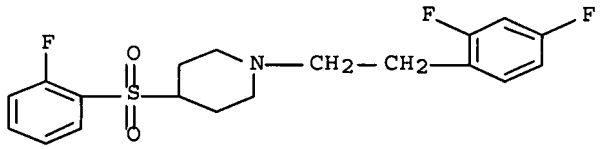
RN 349664-97-7 CAPLUS

CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(2-fluorophenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



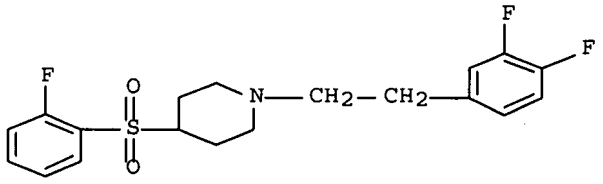
● HCl

RN 349664-98-8 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[(2-fluorophenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



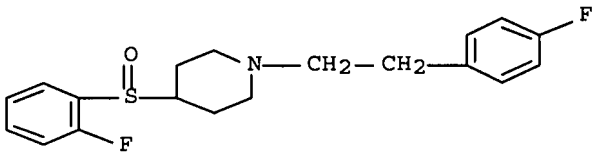
● HCl

RN 349664-99-9 CAPLUS
CN Piperidine, 1-[2-(3,4-difluorophenyl)ethyl]-4-[(2-fluorophenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



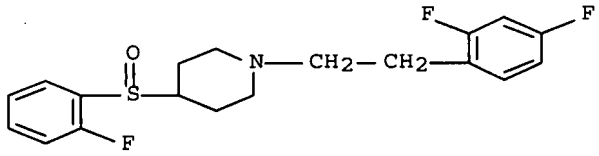
● HCl

RN 349665-03-8 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(2-fluorophenyl)sulfinyl]-, hydrochloride (9CI) (CA INDEX NAME)



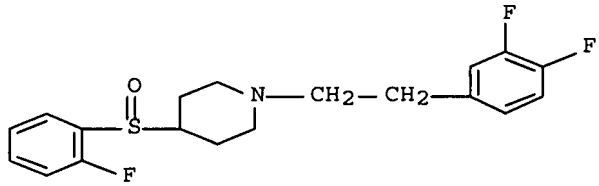
● HCl

RN 349665-04-9 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[(2-fluorophenyl)sulfinyl]-, hydrochloride (9CI) (CA INDEX NAME)



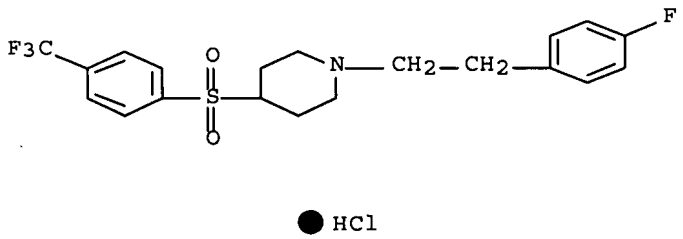
● HCl

RN 349665-05-0 CAPLUS
CN Piperidine, 1-[2-(3,4-difluorophenyl)ethyl]-4-[(2-fluorophenyl)sulfinyl]-, hydrochloride (9CI) (CA INDEX NAME)



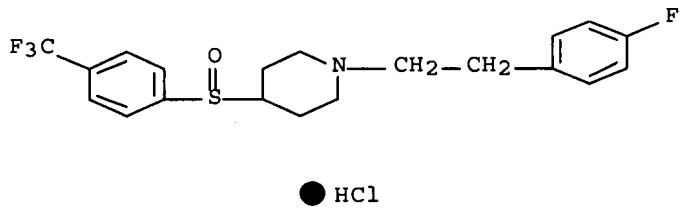
● HCl

RN 349665-06-1 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[[4-(trifluoromethyl)phenyl]sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



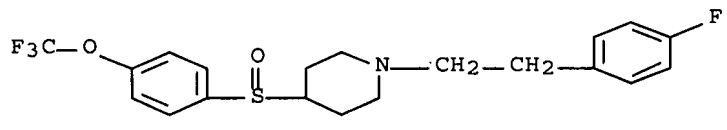
● HCl

RN 349665-07-2 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[[4-(trifluoromethyl)phenyl]sulfinyl]-, hydrochloride (9CI) (CA INDEX NAME)



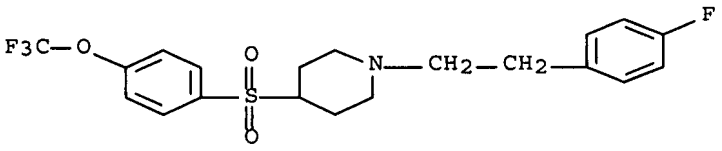
● HCl

RN 349665-08-3 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[[4-(trifluoromethoxy)phenyl]sulfinyl]-, hydrochloride (9CI) (CA INDEX NAME)

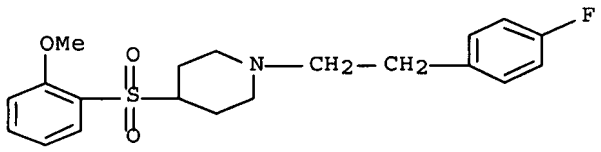


● HCl

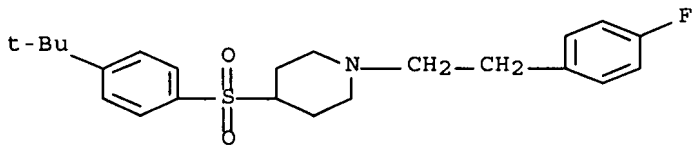
RN 349665-09-4 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[[4-(trifluoromethoxy)phenyl]sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



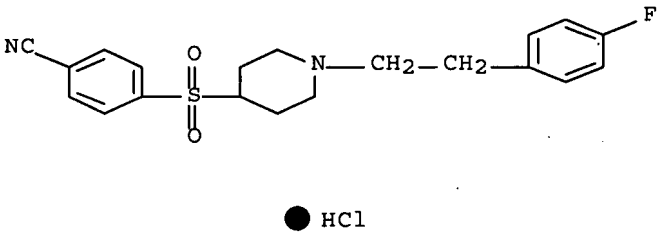
RN 349665-10-7 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[(2-methoxyphenyl)sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)



RN 349665-12-9 CAPLUS
CN Piperidine, 4-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

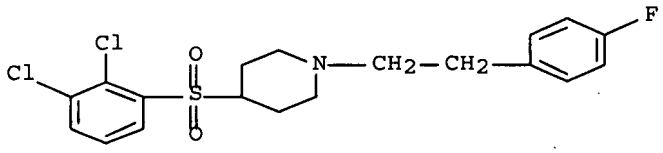


RN 349665-14-1 CAPLUS
CN Benzonitrile, 4-[[1-[2-(4-fluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



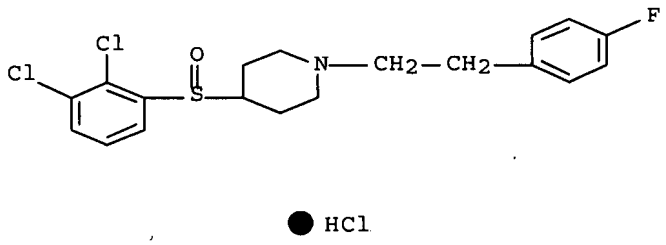
● HCl

RN 349665-17-4 CAPLUS
CN Piperidine, 4-[(2,3-dichlorophenyl)sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

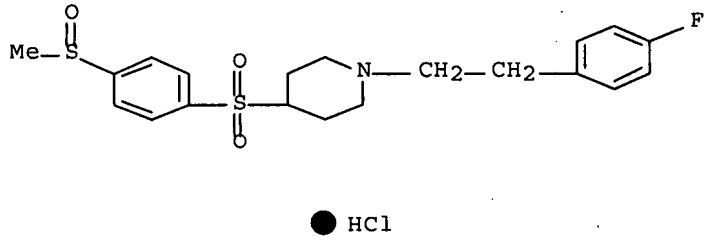


● HCl

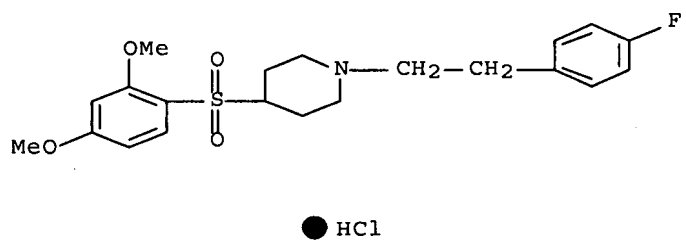
RN 349665-18-5 CAPLUS
CN Piperidine, 4-[(2,3-dichlorophenyl)sulfinyl]-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



RN 349665-25-4 CAPLUS
CN Piperidine, 1-[2-(4-fluorophenyl)ethyl]-4-[[4-(methylsulfinyl)phenyl]sulfonyl]-, hydrochloride (9CI) (CA INDEX NAME)

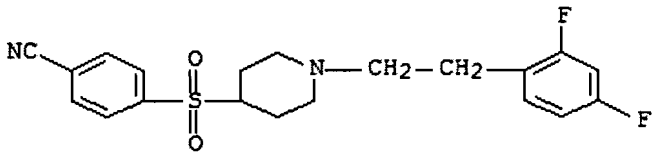


RN 349665-29-8 CAPLUS
CN Piperidine, 4-[(2,4-dimethoxyphenyl)sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-
, hydrochloride (9CI) (CA INDEX NAME)

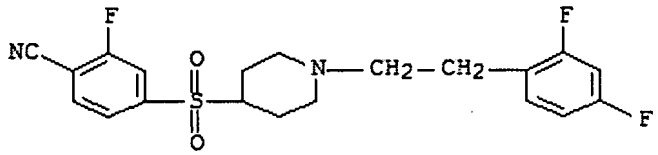


Blurton, et. al. WO 2000/043362 teaches the following compounds:

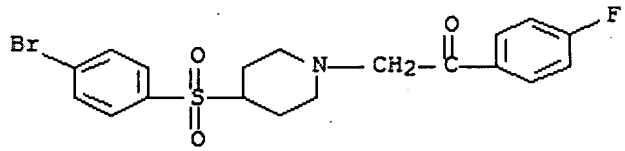
RN 285994-62-9 CAPLUS
CN Benzonitrile, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-
(9CI) (CA INDEX NAME)



RN 285994-66-3 CAPLUS
CN Benzonitrile, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-
2-fluoro- (9CI) (CA INDEX NAME)



RN 285994-96-9 CAPLUS
CN Ethanone, 2-[4-[(4-bromophenyl)sulfonyl]-1-piperidinyl]-1-(4-fluorophenyl)-
(9CI) (CA INDEX NAME)

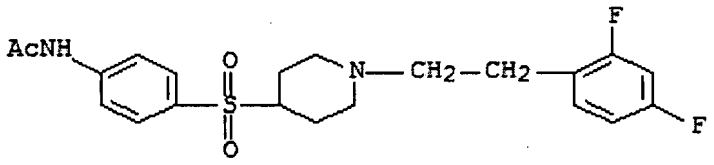


IT 285994-64-1P 285994-68-5P 285994-70-9P

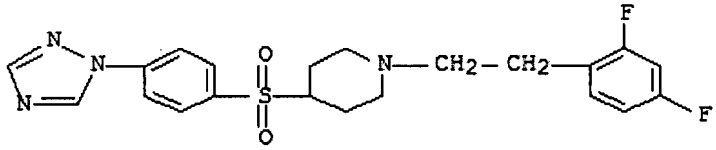
(prepn. of phenylsulfonyl derivs. as 5-HT receptor ligands)

RN 285994-64-1 CAPLUS

CN Acetamide, N-[4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

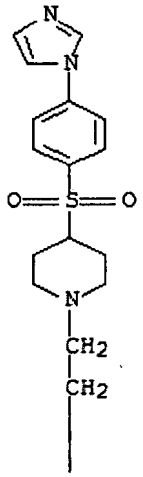


RN 285994-68-5 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(1H-1,2,4-triazol-1-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

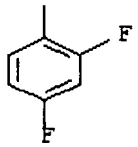


RN 285994-70-9 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(1H-imidazol-1-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

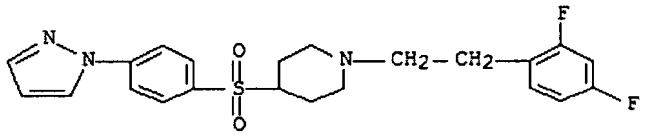
PAGE 1-A



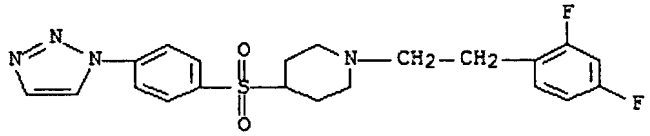
PAGE 2-A



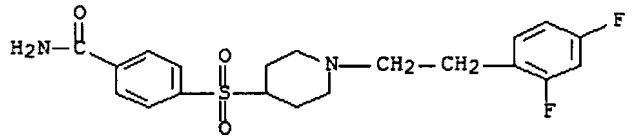
RN 285994-72-1 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(1H-pyrazol-1-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



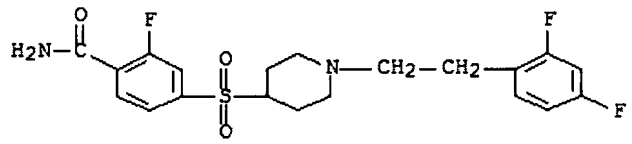
RN 285994-73-2 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(1H-1,2,3-triazol-1-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



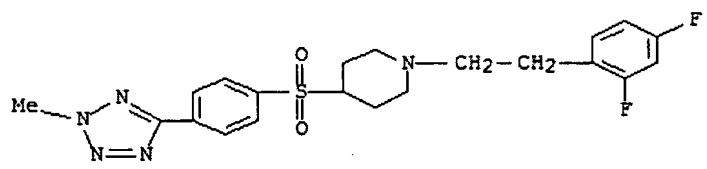
RN 285994-74-3 CAPLUS
CN Benzamide, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



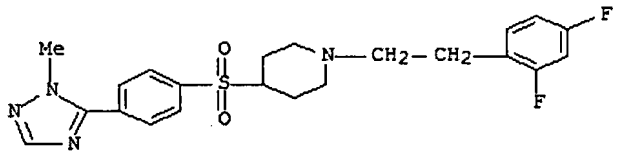
RN 285994-76-5 CAPLUS
CN Benzamide, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-2-fluoro- (9CI) (CA INDEX NAME)



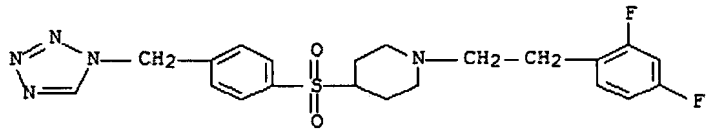
RN 285994-78-7 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(2-methyl-2H-tetrazol-5-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



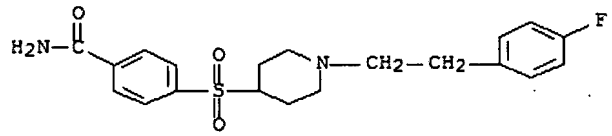
RN 285994-80-1 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



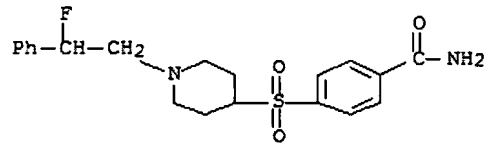
RN 285994-82-3 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-[[4-(1H-tetrazol-1-ylmethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



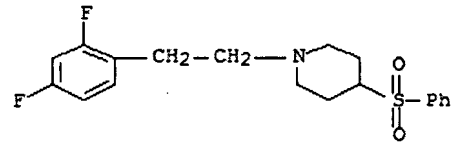
RN 285994-86-7 CAPLUS
CN Benzamide, 4-[[1-[2-(4-fluorophenyl)ethyl]-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



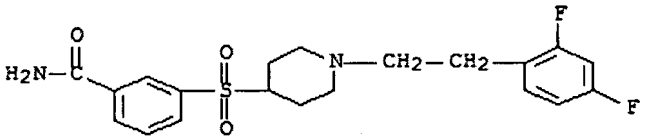
RN 285994-90-3 CAPLUS
CN Benzamide, 4-[[1-(2-fluoro-2-phenylethyl)-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



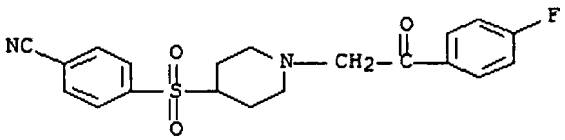
RN 285994-92-5 CAPLUS
CN Piperidine, 1-[2-(2,4-difluorophenyl)ethyl]-4-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



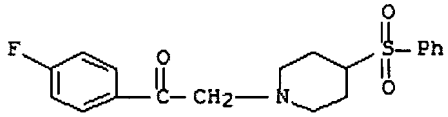
RN 285994-94-7 CAPLUS
CN Benzamide, 3-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 285994-98-1 CAPLUS
CN Benzonitrile, 4-[[1-[2-(4-fluorophenyl)-2-oxoethyl]-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

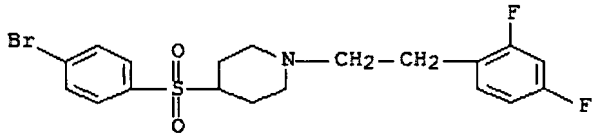


RN 285994-99-2 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-[4-(phenylsulfonyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



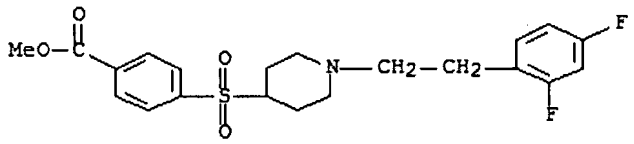
IT 285995-02-0P 285995-03-1P 285995-04-2P
285995-07-5P 285995-08-6P 285995-09-7P
285995-10-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of phenylsulfonyl derivs. as 5-HT receptor ligands)

RN 285995-02-0 CAPLUS
CN Piperidine, 4-[(4-bromophenyl)sulfonyl]-1-[2-(2,4-difluorophenyl)ethyl]- (9CI) (CA INDEX NAME)

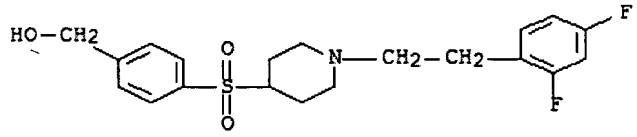


RN 285995-03-1 CAPLUS
CN Benzoic acid, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

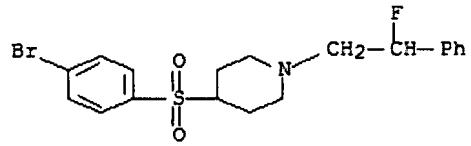
RN 285995-03-1 CAPLUS
CN Benzoic acid, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



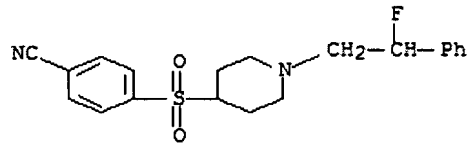
RN 285995-04-2 CAPLUS
CN Benzenemethanol, 4-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



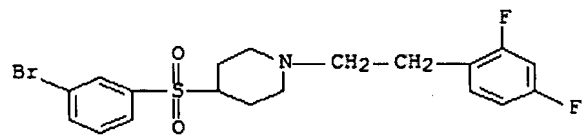
RN 285995-07-5 CAPLUS
CN Piperidine, 4-[(4-bromophenyl)sulfonyl]-1-(2-fluoro-2-phenylethyl)- (9CI) (CA INDEX NAME)



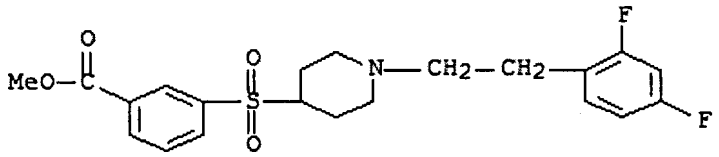
RN 285995-08-6 CAPLUS
CN Benzonitrile, 4-[[1-(2-fluoro-2-phenylethyl)-4-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 285995-09-7 CAPLUS
CN Piperidine, 4-[(3-bromophenyl)sulfonyl]-1-[2-(2,4-difluorophenyl)ethyl]- (9CI) (CA INDEX NAME)

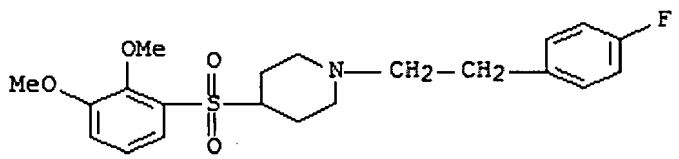


RN 285995-10-0 CAPLUS
CN Benzoic acid, 3-[[1-[2-(2,4-difluorophenyl)ethyl]-4-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

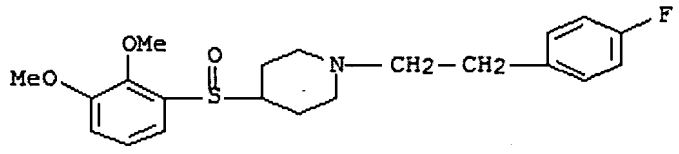


Wang teaches the following compounds:

RN 403848-68-0 CAPLUS
CN Piperidine, 4-[(2,3-dimethoxyphenyl)sulfonyl]-1-[2-(4-fluorophenyl)ethyl]-(9CI) (CA INDEX NAME)



RN 403848-70-4 CAPLUS
CN Piperidine, 4-[(2,3-dimethoxyphenyl)sulfinyl]-1-[2-(4-fluorophenyl)ethyl]-(9CI) (CA INDEX NAME)



Patani teaches that the exact bioisosteric replacement seen here (H to F) is well known and the art:

> **"II. Classical Bioisosteres A. Monovalent Atoms or Groups**
> Similarities in certain physicochemical properties have enabled investigators to successfully exploit several monovalent bioisosteres. These can be divided into the following groups: (1) fluorine vs hydrogen replacements; (2) amino-hydroxyl interchanges; (3) thiol-hydroxyl interchanges; (4) fluorine, hydroxyl, amino, and methyl group interchanges (Grimm's Hydride

Displacement Law); (5) chloro, bromo, thiol, and hydroxyl group interchanges (Erlenmeyer's Broadened Classification of Grimm's Displacement Law).
1. Fluorine vs Hydrogen Replacements
The substitution of hydrogen by fluorine is one of the more commonly employed monovalent isosteric replacements." Patani et. al. pg. 3149.

Ascertainment of the difference between the prior art and the claims

It is clear that the prior compounds differ only from the compounds of the instant case by the position of the fluorine atom or alternatively the replacement of a hydrogen with a fluorine.

Finding of prima facie obviousness

Rational and Motivation

(MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare position isomers or bioisosteres of those of Ackermann, Blurton, Fletcher, or Wang to produce the instant invention. Positional isomers, having the same radical on different positions of the molecule, are *prima facie* obvious, and require no secondary teaching. The experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these position isomers based on the expectation that such close analogues would have similar properties and upon the routine nature of such position isomer experimentation in the art of medicinal chemistry. Indeed it is clear that these compounds have exactly the same properties as those of Ackermann, Blurton, Fletcher, or Wang, namely activity at the 5-HT2a receptor. It would be routine for the chemist to vary the point of attachment in order to increase potency and to establish better patent protection for her compounds. *In re JONES* 74 USPQ 152 (4-methyl naphthyl-1-acetic acid and 2-methyl naphthyl-1-acetic acid obvious over a reference teaching 1-methyl naphthyl-2-acetic acid), quoted with approval by *Ex parte MOWRY AND SEYMOUR* 91 USPQ 219, *Ex parte Ullyot* 103 USPQ 185 (4-hydroxy-1-oxo-1,2,3,4-tetrahydroisoquinoline obvious over a reference teaching 4-hydroxy-2-oxo-1,2,3,4-tetrahydroquinoline), "[p]osition isomers are recognized by chemists as similar materials", *Ex parte BIEL* 124 USPQ 109 (N-ethyl-3-piperidyl diphenylacetate obvious

over a reference teaching N-alkyl-4-piperidyl diphenylacetate), "[appellant's arguments] do not, in any way, obviate the plain fact that appellant's DACTIL is an isomer of McElvain et al.'s compound. This close relationship places a burden on appellant to show some unobvious or unexpected beneficial properties in his compound in order to establish patentability", *Ex parte Henkel* 130 USPQ 474, (1-phenyl-3-methyl-4-hydroxypyrazole obvious over reference teaching 3-phenyl-5-methyl-4-hydroxypyrazole), "appellants have made no comparative showing here establishing the distinguishing characteristics they allege which we might consider as evidence that the claimed compounds are unobvious. It is clear from *In re Henze*, supra, and the authorities it cites, that at least this much is necessary to establish patentability in adjacent homologs and **position isomers** (emphasis added)".

In re Surrey 138 USPQ 67, (2,6-dimethylphenyl-N-(3-dimethylaminopropyl) carbamate obvious over a reference teaching 2,4-dimethylphenyl N-(3-dimethylaminopropyl) carbamate), *In re MEHTA* 146 USPQ 284, (2-(1-methyl)-pyrrolidylmethyl benzilate obvious over a reference teaching 3-(1-methyl)-pyrrolidylmethyl benzilate), "[t]he fact that a **position isomer** (emphasis added) of a compound is known is some evidence of the obviousness of that compound. **Position isomerism** (emphasis added) is a fact of close *structural* (emphasis in original) similarity ...".*Deutsche Gold-Und Silber-Scheideanstalt Vormals Roessler v. Commissioner of Patents*, 148 USPQ 412, (1-azaphenothiazines obvious over references teaching 2-azaphenothiazines, 3-azaphenothiazines, and 4-azaphenothiazines), *In re Crounse*, 150 USPQ 554 (dye with *para* ($CONH_2$) and *ortho* (OCH_3) obvious over a dye with the same nucleus and *meta* ($CONH_2$) and *para* (OCH_3) group), *Ex parte Allais*, 152 USPQ 66, (3-□-aminopropyl-6-methoxyindole obvious over a reference teaching 3-□-aminopropyl-5-methoxyindole), *In re Wiechert* 152 USPQ 247, (1-methyl dihydrotestosterones obvious over a reference teaching 2-methyl dihydrotestosterones), *Monsanto Company v. Rohm and Haas Company*, 164 USPQ 556, at 559, (3',4'-dichloropropionanilide obvious over references teaching 2',4'-dichloropropionanilide and 2',5'-dichloropropionanilide), *Ex parte Naito and Nakagawa*, 168 USPQ 437, (3-phenyl-5-alkyl-isothiazole-4-carboxylic acid obvious over a reference teaching 5-phenyl-3-alkyl-isothiazole-4-carboxylic acid), "[t]his merely involves **position isomers** (emphasis added) and under the decisions cited, the examiner's holding of *prima facie* obviousness is warranted." *In re Fouche*, 169 USPQ 429, (10-aliphatic substituted derivatives of

dibenzo[a,d]cycloheptadiene obvious over reference teaching 5-aliphatic substituted derivatives of dibenzo[a,d]cycloheptadiene). *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ullyot*, 103 USPQ 185, which found a *prima facia* case of of 2-oxo-quinolines obvious over prior art a 1-oxo-isoquinoline, *In re FINLEY,* 81 USPQ 383, 2-ethyl hexyl salicylate over octyl salicylate.

Ex parte Engelhardt, 208 USPQ 343 at 349, "[i]f functional groups capable of withdrawing or repelling electrons are located in the chain or **ring** (emphasis added) of a biologically active compound, transfer of such groups to other positions in which their electronic effects are lessened or enhanced may alter the biological activity of the modified compound. Hence, **position isomerism** (emphasis added) has been used as a tool to obtain new and useful drugs", *In re Grabiak* 226 USPQ 870, "[w]hen chemical compounds have "very close" structural similarities and similar utilities, without more a *prima facie* case may be made", *In re Deuel* 34 USPQ2d 1210, "a known compound may suggest its analogs or isomers, either geometric isomers (*cis* v. *trans*) or **position isomers** (emphasis added) (*e.g. ortho v. para*)".

The bioisosteric replacement of H with F, was well known at the time the invention was made as evidience by Patani et. al. Moreover by looking at the structure of the compounds of Ackermann, Blurton, and Fletcher in particular it is clear that polyfluorinated compounds were the preferred compounds of these inventions. *In re Grabiak* 226 USPQ 870, "[w]hen chemical compounds have "very close" structural similarities and similar utilities, without more a *prima facie* case may be made", *In re Deuel* 34 USPQ2d 1210, "a known compound may suggest its **analogs** or isomers, either geometric isomers (*cis* v. *trans*) or **position isomers** (*e.g. ortho v. para*) (emphasis added) ". *Ex parte Dole* 119 USPQ 260, where a tetrachloro compound was held unpatentably obvious over the dichloro analog, shown in Figure 1.

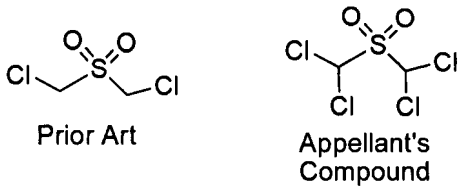


Figure 1. Structures of Ex Parte Dole.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One of ordinary skill is also one of "ordinary creativity, not an automaton". See Leapfrog Enterprises Inc. v. Fisher-Price. and Mattel Inc. UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT "An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at 12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Objections

5. Claim 11 is drawn to compounds where the Ar ring is either bezisothiazolyl-3-yl or benzothiophenyl-3-yl and is objected to for depending from a rejected base claim, but would be allowable if put in proper dependent format.

6. Claim 15 is objected to for the following informalities: It appears that the "p" of piperidine was mistakenly deleted from several compound names. This occurs at a carriage return when the compound name is longer than one line. Appropriate correction is required.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571) 272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Primary examiner, Rita Desai can be reached on (571)272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

R Desai 10/2/07

RITA DESAI
PRIMARY EXAMINER